REMARKS

Amendments

Claims 6, 8, 9, 23, 29-32 and 35-39 are under consideration in the instant Office Action. Claims 23, 29 and 30 have been amended. The amendments to the claims do not constitute new matter and are completely supported throughout the specification and originally filed claims.

The foregoing amendments are made solely to expedite prosecution of the application and are not intended to limit the scope of the invention. Further, the amendments to the claims are made without prejudice to the pending or now canceled claims or to any subject matter pursued in a related application. The Applicant reserves the right to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation, or continuation-in-part application.

Objections

Claim 29 has been objected to for recitation of "claim-6." The claim has been amended to correct the typographical error.

Rejections

Rejections under 35 U.S.C. §§ 101/112 – 1st paragraph

The Examiner has rejected claims 6, 8, 9, 23, 29-32 and 35-39 under 35 U.S.C. § 101 because the claimed invention is allegedly not supported by either a specific or substantial asserted utility or a well-established utility. Applicant respectfully traverses the rejection.

According to 35 U.S.C. § 101, "[w]hoever invents . . . any new and useful . . . composition of matter may obtain a patent therefore. . . . "

Under the Patent Office's Utility Requirement Guidelines:

> If at any time during the examination, it becomes readily apparent that the claimed invention has a well-established utility, do not impose a rejection based on lack of utility. An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible.
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> If the applicant has asserted that the claimed invention is useful for any particular practical purpose (i.e., it has a "specific and substantial utility") and the assertion

would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility.

(emphasis added)(MPEP § 2107, II (A)(3); II (B)(1)). Thus, according to Patent Office guidelines, a rejection for lack of utility may not be imposed where an invention has either a well-established utility or is useful for a particular practical purpose. The present invention satisfies either standard.

The present invention has a well-established utility since a person of ordinary skill in the art "would immediately appreciate why" knockout mice are useful. As a general principle, any knockout mouse has the inherent and well-established utility of defining the function and role of the disrupted target gene, regardless of whether the inventor has described any specific phenotypes, characterizations or properties of the knockout mouse. The sequencing of the human genome has produced countless genes whose function has yet to be determined. According to the National Institute of Health, knockout mice represent a critical tool in studying gene function:

> Over the past century, the mouse has developed into the premier mammalian model system for genetic research. Scientists from a wide range of biomedical fields have gravitated to the mouse because of its close genetic and physiological similarities to humans, as well as the ease with which its genome can be manipulated and analyzed.
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> In recent decades, researchers have utilized an array of innovative genetic technologies to produce custom-made mouse models for a wide array of specific diseases, as well as to study the function of targeted genes. One of the most important advances has been the ability to create transgenic mice, in which a new gene is inserted into the animal's germline. Even more powerful approaches, dependent on homologous recombination, have permitted the development of tools to "knock out" genes, which involves replacing existing genes with altered versions; or to "knock in" genes, which involves altering a mouse gene in its natural location. To preserve these extremely valuable strains of mice and to assist in the propagation of strains with poor reproduction, researchers have taken advantage of state-of-the-art reproductive technologies, including cryopreservation of embryos, in vitro fertilization and ovary transplantation.

(http://www.genome.gov/pfv.cfm?pageid=10005834) (emphasis added). Thus, the knockout mouse has been accepted as one of the premier models for determining gene function, a utility that is specific, substantial and credible.

Commercial use and acceptance is one important indication that the utility of an invention has been recognized by one of skill in the art ("A patent system must be related to the world of commerce rather than to the realm of philosophy." Brenner v Manson, 383 U.S. 519, 148 U.S.P.Q. 689, 696 (1966)). Commercial use of the knockout mice produced by Assignee Deltagen has been clearly established. Deltagen has created a database comprising characteristics derived from approximately 750 lines of knockout mice. Three of the largest pharmaceutical companies in the world, Merck, Pfizer and GSK, have subscribed to the database and requested access to the lines of mice for the purpose of studying gene function. In fact, all three institutions have ordered the presently claimed FPR-RS4 knockout mouse invention. This commercial acceptance more than satisfies the practical utility requirement of section 101.

Applicant respectfully submits that this is not the case where a composition of matter is itself being studied in order to establish a utility for the composition. Rather, the knockout mouse is being studied to determine the function of the target gene. This case is clearly separate and distinct from the situation referred to in Brenner v. Manson (383 U.S. 519, 148 U.S.P.Q. 689, 696 (1966))(We find absolutely no warrant for the proposition that although Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing, a different set of rules was meant to apply to the process which yielded the unpatentable product). The dicta in Brenner related to the patentability of a chemical compound which itself had no known use. Thus, the utility could not solely consist of testing the compound in order to determine a utility for the compound itself. In the present case, the FPR-RS4 knockout mouse is being used to study the utility and function of the FPR-RS4 gene, and not for the purpose of establishing a utility for the mouse. The distinction is clear: one skilled in the art would not understand what to do with a compound without a defined use, but would immediately recognize the use of a knockout mouse having a specific gene disruption.

The present case of mouse knockouts may be appropriately analogized to other research tools, with respect to which the Patent Office has commented:

> Some confusion can result when one attempts to label certain types of inventions as not being capable of having a specific and substantial utility based on the

> setting in which the invention is to be used. One example is inventions to be used in a research or laboratory setting. Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have a clear, specific and unquestionable utility (e.g., they are useful in analyzing compounds). An assessment that focuses on whether an invention is useful only in a research setting thus does not address whether the invention is in fact "useful" in a patent sense. Instead, Office personnel must distinguish between inventions that have a specifically identified substantial utility and inventions whose asserted utility requires further research to identify or reasonably confirm. Labels such as "research tool," "intermediate" or "for research purposes" are not helpful in determining if an applicant has identified a specific and substantial utility for the invention.

(MPEP § 2107.01, I). As with gas chromatographs, screening assays and nucleotide sequencing techniques, knockout mice have a clear, specific and unquestionable utility (e.g., they are useful in analyzing gene function).

Applicant submits that since one of ordinary skill in the art would immediately recognize the utility of a knockout mouse in studying gene function, a utility which is specific, substantial and credible, the invention has a well-established utility, thus satisfying the utility requirement of section 101. On this basis alone, withdrawal of the rejection with respect to the present invention is warranted, and respectfully requested.

In addition, the claimed invention is useful for a particular purpose. The Applicant has demonstrated and disclosed specific phenotypes of the presently claimed mice, i.e., increased anxiety, decreased coordination or decreased susceptibility to seizure. Utility of a knockout mouse demonstrating any of these properties would be apparent to, and considered credible by, one of skill in the art.

The Examiner argues that the phenotypes appear to be generic rather than specific to any disease, and that the specification fails to teach a role or function for FPR-RS4 that correlates to any disease or disorder related to any of the claimed phenotypes.

Applicant respectfully disagrees. Anxiety disorders are a well-recognized condition which are the subject of drug development studies and treatment strategies. For example, there are currently in excess of sixty (60) clinical trials enrolling patients for the study of anxiety disorders (http://clinicaltrials.gov/ct/screen/BrowseAny?path=%2Fbrowse%2Fby-condition%2Faz%2FA%2FD001008%2BAnxiety%2BDisorders&recruiting=true). The intense interest in studying treatments for anxiety disorders establishes that the phenotype and the

disease/disorder are one and the same. Establishment of a correlation between the phenotype and the disease/disorder is unnecessary and unwarranted.

The claimed knockout mouse demonstrates a role for FPR-RS4 in anxiety disorders. Therefore, FPR-RS4 correlates with a specific disorder. In addition, the utility of a knockout mouse demonstrating increased anxiety has been recognized as a useful tool in the discovery of anxiolytics. For example, Mombereau *et al.* (Neuropsychopharmacology (2004) 29, 1050-62)(copy attached) discloses a $GABA_B$ receptor knockout having increased anxiety. Based on observations in the knockout mouse and subsequent pharmacological experiments using receptor antagonists, the authors proposed that the $GABA_B$ receptor serve as a novel therapeutic strategy for the development of anxiolytics.

The Examiner cites Belzung *et al.* (Behavioral Brain Research, 125, 141-149 (2001)) for the proposition that a single gene disruption cannot be clearly correlated to the disease state of anxiety. Whether anxiety disorders are correlated with a single or multiple genes is not relevant to the issue of utility of a single gene or its corresponding knockout mouse. The fact that other genes may be involved does not detract from the importance of FPR-RS4 or its expression product as a potential target for drug development. To satisfy the utility requirement, an invention need not be the best or only tool available. It need only be useful.

Moreover, Belzung *et al.* does not stand for, nor can it support, the proposition that a knockout mouse demonstrating anxiety has no utility or use. The reference discusses the relative utility of so-called 'pathological' anxiety models and 'state' anxiety models. Nowhere in the reference do the authors state that knockout mice have no use or utility, only that they may not be the best or only tools available. Applicant respectfully points out that the standard is not superiority of use over existing tools or compositions. It suffices that the claimed invention has utility.

In fact, Belzung *et al.* acknowledge the utility of knockout mice demonstrating increased anxiety. For example, the authors in discussing the 5-HT_{1A} receptor deficient mouse, which demonstrated anxiety related behavior, comment that "[t]here is not doubt for example that the 5-HT_{1A} receptor plays a role in anxiety, but it is excessive to describe mice lacking this receptor as 'an animal model of anxiety-related disorder' since it is by far not the only target involved in emotional processes." (Belzung at 146)(emphasis added). Thus, because these phenotypes were observed in the knockout mouse, the function of the 5-HT_{1A} receptor was determined. That the

receptor is not the only gene involved in anxiety disorders is irrelevant to whether the knockout mouse has utility.

Belzung concludes that:

> While animal models of 'state' anxiety remain the mainstay of tests used in studies dealing with emotional processes, models of 'pathological' anxiety, which are in great part based on the use of gene targeting technology, are used increasingly. However, their usefulness as models of anxiety is limited since they are based on the deletion of a single gene, which alone can hardly account for a complex condition such as anxiety.

(Belzung at 147)(emphasis added). Again, Belzung acknowledges the increasing use (i.e., utility) of knockout mice in the study of anxiety. Their view that more than one gene is involved in such disorders is not relevant to the issue of the patentable utility of a knockout mouse.

The above discussion with respect to anxiety disorders equally applies to the phenotypes of impaired coordination and abnormal seizure susceptibility exhibited by the claimed mice. (Applicants respectfully point out that a claimed invention need only meet one of its stated objectives to comply with the utility requirement (Raytheon Co. v. Roper Corp., 724 F.2d 951, 220 U.S.P.Q. 592 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 835, 225 U.S.P.Q. 232 (1984)). Applicant believes that any of the cited phenotypes alone would satisfy the practical purpose component of utility guidelines, and that the utility of each phenotype need not be separately argued). A phenotype of impaired coordination resulting from disruption of FPR-RS4 relates to motor function and coordination problems, and seizure disorders are a recognized disorder. These phenotypes indicate a role for FPR-RS4 in these conditions, and establishes the utility of the mice as models for such conditions or disorders, as well as for discovering appropriate treatments.

In summary, Applicant submits that the claimed FPR-RS4 knockout mouse, regardless of any disclosed phenotypes, has inherent and well-established utility in the study of the function of the FPR-RS4 gene, and thus satisfies the utility requirement of section 101. Moreover, Applicant believes that the specific phenotypes of the transgenic mice demonstrate that the mice are useful for a specific practical purpose that would be readily understood by and considered credible by one of ordinary skill in the art.

In light of the arguments set forth above, Applicant does not believe that the Examiner has properly established a *prima facie* showing that establishes that it is more likely than not that a person of ordinary skill in the art would not consider that any utility asserted by the Applicant would be specific and substantial. (MPEP § 2107). Withdrawal of the rejections is therefore respectfully requested.

The Examiner has also rejected claims 6, 8, 9, 23, 29-32 and 35-39 under 35 U.S.C. § 112, first paragraph, because one skilled in the art would allegedly not know how to use the transgenic mice as a result of the alleged lack of either a specific or substantial asserted utility or a well-established utility set forth in the above utility rejection. Applicants respectfully traverse the rejection. For reasons set forth above, the claimed invention satisfies the utility requirement of section 101, and therefore one of skill in the art would know how to use the invention. Withdrawal of the rejection is respectfully requested.

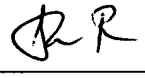
In addition, the Examiner has rejected claims 23 and 30. The claims have been amended in accordance with the Examiner's comments. Withdrawal of the rejections is respectfully requested.

It is submitted that the claims are currently in condition for allowance, and notice to that effect is respectfully requested. The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 13-2725.

In view of the above amendments and remarks, Applicant respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

8-26-04
Date



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